

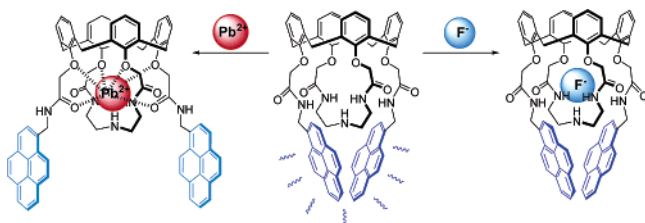
Bifunctional Fluorescent Calix[4]arene Chemosensor for Both a Cation and an Anion

Ji Yeon Lee,[†] Sung Kuk Kim,[†] Jong Hwa Jung,[‡] and Jong Seung Kim^{*,†}

Department of Chemistry, Institute of Nanosensor and Biotechnology, Dankook University, Seoul 140-714, Korea, and Korea Basic Science Institute (KBSI), Daejeon 305-333, Korea

jongskim@dankook.ac.kr

Received October 8, 2004



A new fluorogenic cone calix[4]triazacrown-5 (**1**) bearing two pyrene amide groups and its structural analogue **2** have been prepared. Excited at 343 nm, **1** and **2** reveal excimer emissions at 448 and 472 nm, respectively. When heavy metal ions such as Pb^{2+} and Co^{2+} are bound to **1**, the fluorescence intensities of both monomer and excimer are quenched whereas H bonding-assisted F^- binding to **1** gives rise to a quenched monomer emission with little excimer emission change.

Selective signaling of heavy metal ions and anions has been a very important topic for the detection and treatment of the toxic metal ions in various chemical systems including living systems. There are, however, relatively few examples of designed sensors for the heavy metal ion in comparison with the variety of compounds developed for the alkali and alkaline earth metal ions.

On account of their high sensitivity and selectivity,^{1–6} fluorescent chemosensors can be effectively used as a tool to analyze and clarify such roles of charged chemical species in living system as well as to measure the amount of metal ions from the sources contaminated with them. Linkage of fluorogenic compounds to appropriately functionalized calix[4]arenes as ion receptors has afforded

such efficient fluorescence chemosensors possessing abilities to selectively sense specific chemical species.⁷

Calix[4]arenes as host molecules for anions or cations have been of particular interest for the following two different reactive sites: (1) phenolic OHs (lower rim) and (2) para positions (upper rim) to the hydroxy groups, which can be readily functionalized by various cation-ligating groups such as carboxylic acid, amides, crown ether, and azacrown ether.^{8,9} In particular, amide groups as a functional group are known to capture not only cations through carbonyl oxygen atoms¹⁰ but also anions through the hydrogen bonding between anions and the acidic hydrogen atoms on nitrogen atoms.¹¹

Most calixarene-based fluorescence sensors have been designed on the photoinduced mechanism inducing the photophysical changes upon ion binding: PET (photoinduced electron transfer),⁷ PCT (photoinduced charge transfer),¹² excimer/exciple formation and extinction,¹³ or energy transfer.¹⁴ Recently, we reported on the fluorescent calix[4]crowns bearing two facing amide groups as a PET-utilizing chemosensor,^{10b} in which the amide groups form complex with a metal ion such as Pb^{2+} , but not with any anions. In a continuation of development of metal ion sensing materials, we herein report pyrene-appended calix[4]triazacrown (**1**) bearing four amide groups capable of sensing anions as well as metal cations.

Scheme 1 shows a synthetic route for the fluorogenic chemosensors **1** and **2** (Figure 1). Calix[4]triazacrown-5

(7) (a) Aoki, I.; Sakaki, T.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1992**, 730. (b) Jin, T.; Ichikawa, K.; Koyama, T. *J. Chem. Soc., Chem. Commun.* **1992**, 499. (c) Ji, H.-F.; Brown, G. M.; Dabestani, R. *Chem. Commun.* **1999**, 609. (d) Kim, J. S.; Shon, O. J.; Rim, J. A.; Kim, S. K.; Yoon, J. *J. Org. Chem.* **2002**, 67, 2348. (e) Kim, J. S.; Noh, K. H.; Lee, S. H.; Kim, S. K.; Kim, S. K.; Yoon, J. *J. Org. Chem.* **2003**, 68, 597.

(8) (a) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989. (b) Gutsche, C. D. In *Synthesis of Macrocycles: Design of Selective Complexing Agents*; Izatt, R. M.; Christensen, J. J., Eds.; Wiley: New York, 1987; p 93. (c) *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer: Dordrecht, 1991. (d) Böhmer, V.; McKevey, M. A. *Chem. Zeit.* **1991**, 195. (e) Gutsche, C. D. In *Calixarenes, Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: Cambridge, U.K., 1989; Vol. 1.

(9) Andreotti, G. D.; Ugozzoli, F.; Ungaro, R.; Pochini, A. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: New York, 1991; Vol. 4, pp 64–125.

(10) (a) van der Veen, N. J.; Flink, S.; Deij, M. A.; Egberink, R. J. M.; van Veggel, F. C. J. M.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **2000**, 122, 6112. (b) Lee, S. H.; Kim, J. Y.; Kim, S. K.; Lee, J. H.; Kim, J. S. *Tetrahedron* **2004**, 60, 5171. (c) Nomura, E.; Takagaki, M.; Nakaoka, C.; Taniguchi, H. *J. Org. Chem.* **2000**, 65, 5932. (d) Nomura, E.; Takagaki, M.; Nakaoka, C.; Uchida, M.; Taniguchi, H. *J. Org. Chem.* **1999**, 64, 3151. (e) Métivier, R.; Leray, I.; Valeur, B. *Chem. Commun.* **2003**, 996.

(11) (a) Ayling, A. J.; Pérez-Payán, M. N.; Davis, A. P. *J. Am. Chem. Soc.* **2001**, 123, 12716. (b) Choi, K.; Hamilton, A. D. *J. Am. Chem. Soc.* **2001**, 123, 2456. (c) Miyaji, H.; Sessler, J. L. *Angew. Chem., Int. Ed.* **2001**, 40, 154. (d) Jagessar, R. C.; Burns, D. H. *Chem. Commun.* **1997**, 1685. (e) Liao, J.-H.; Chen, C.-T.; Fang, J.-M. *Org. Lett.* **2002**, 4 (4), 561. (f) Gale, P. A.; Chen, Z.; Drew, M. G. B.; Heath, J. A.; Beer, P. D. *Polyhedron* **1998**, 17 (4), 405.

(12) Leray, I.; Lefevre, J.-P.; Delouis, J.-F.; Delaire, J.; Valeur, B. *Chem. Eur. J.* **2001**, 7 (21), 4590.

(13) (a) Nishizawa, S.; Kaneda, H.; Uchida, T.; Teramae, N. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2325. (b) Nishizawa, S.; Kato, Y.; Teramae, N. *J. Am. Chem. Soc.* **1999**, 121, 9463.

(14) Hecht, S.; Vladimirov, N.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2001**, 123, 18.

* Corresponding author. Fax: +82-2-797-3277.

[†] Dankook University.

[‡] Korea Basic Science Institute.

(1) Xie, X. S. *Acc. Chem. Res.* **1996**, 29, 598.

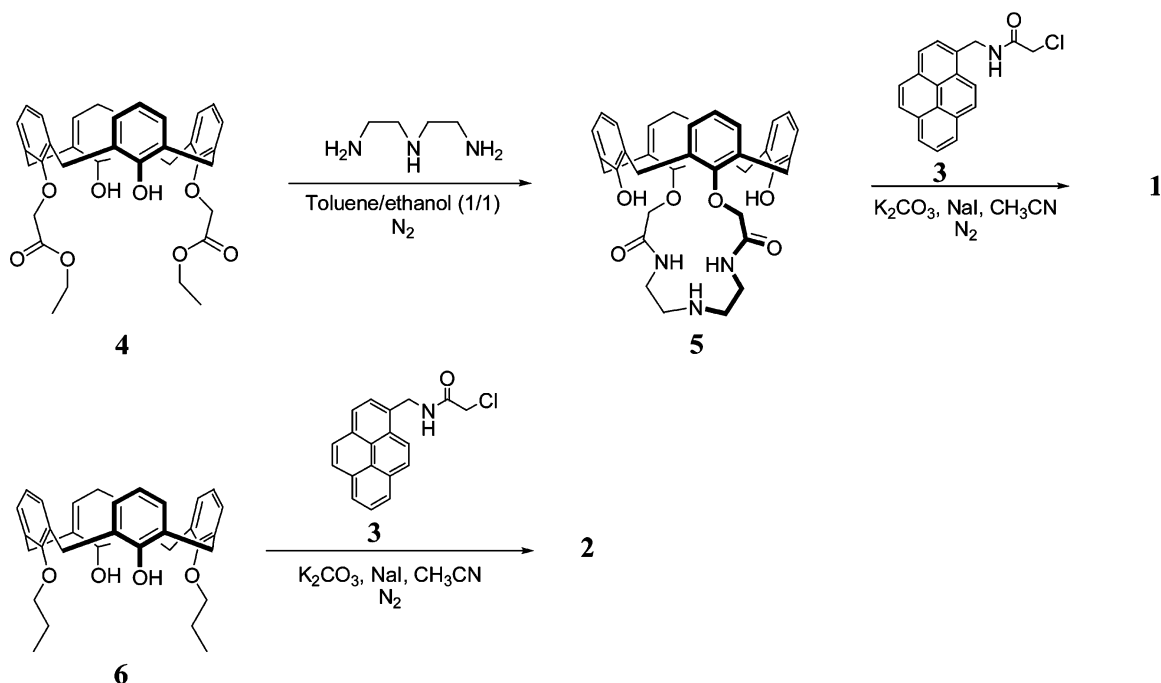
(2) Goodwin, P. M.; Ambrose, W. P.; Keller, R. A. *Acc. Chem. Res.* **1996**, 29, 607.

(3) Orrit, M.; Bernard, J. *Phys. Rev. Lett.* **1990**, 65, 2716.

(4) Mets, U.; Rigler, R. *J. Fluoresc.* **1994**, 4, 259.

(5) (a) Moerner, W. E.; Basche, T. *Angew. Chem., Int. Ed. Engl.* **1993**, 32, 457. (b) Moerner, W. E. *Acc. Chem. Res.* **1996**, 29, 563.

(6) Yeung, E. S. *Acc. Chem. Res.* **1994**, 27, 209.

SCHEME 1. Synthetic Routes for Fluorescent Chemosensors **1** and **2**

(**5**)¹⁵ was prepared in the cone conformation from the reaction of calix[4]arene diester (**4**)¹⁵ and diethylene triamine in a mixture of ethanol and toluene (1:1) as a solvent. Reaction of **5** with *N*-(1-pyrenylmethyl)chloroacetamide (**3**)^{10a} using K_2CO_3 as a base in acetonitrile with a catalytic amount of sodium iodide provided **1** in 51% yield. The 1H NMR spectrum of **1** exhibits two

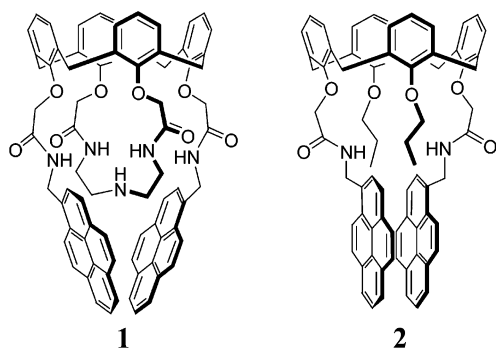


FIGURE 1. Structures of fluorescence chemosensors **1** and **2**.

doublets at 3.79 and 3.29 ppm in AB pattern, corresponding to protons of the methylene bridge, which suggests that **1** be in the cone conformation. A peak at 31.3 ppm in the ^{13}C NMR spectrum provides concrete evidence for its cone conformation. Compound **2** having propyl groups instead of the triazacrown ring was synthesized by the reaction of 25,27-dipropoxy calix[4]arene (**6**)¹⁶ with **3** in the presence of K_2CO_3 in acetonitrile with a catalytic amount of sodium iodide. Detailed synthetic procedures

(15) No, K.; Lee, H. J.; Park, K. M.; Lee, S. S.; Noh, K. H.; Kim, S. K.; Lee, J. Y.; Kim, J. S. *J. Heterocycl. Chem.* **2004**, *41*, 211.

(16) (a) Kim, J. S.; Lee, W. K.; No, K. H.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **2000**, *41*, 3345. (b) Koh, K. N.; Araki, K.; Shinkai, S.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1995**, *36*, 6095.

TABLE 1. Fluorescence Changes ($I - I_0$) of **1** and **2** upon Addition of Various Metal Ions^a

| ligand | λ_{em} (nm) | fluorescence changes ($I - I_0$) | | | | | |
|----------|---------------------|------------------------------------|-----------------|----------------|-----------------|------------------|------------------|
| | | Li ⁺ | Na ⁺ | K ⁺ | Cs ⁺ | Pb ²⁺ | Co ²⁺ |
| 1 | 396 | 76 | 7.0 | 1.0 | -3.0 | -17 | -168 |
| | 448 | -74 | 26 | 23 | -223 | -242 | |
| 2 | 396 | -64 | -29 | 11 | -3.0 | -103 | -92 |
| | 472 | 29 | 66 | 15 | 18 | -352 | -194 |

^a Conditions: **1** and **2**, 6.0 μ M in CH_3CN , excitation at 343 nm; metal ions, 500 equiv in CH_3CN . I_0 : fluorescence emission intensity of free **1** and **2**. I : fluorescence emission intensity of metal-ion-complexed **1** and **2**.

and their physical properties including the conformation are described in the Supporting Information.

Compound **2** displays an excimer emission at 472 nm whereas **1** emits at 448 nm, in which 24 nm blue shifting of **1** is attributable to the fact that two pyrenes of **1** are less overlapped because of a steric hindrance of the triazacrown ring across the two pyrene pendants. This finding is also comparable to those found in the compound having a simple crown-5 or -6 instead of a triazacrown ring, in which the two pyrene groups form neither an intramolecular nor an intermolecular excimer.^{10b} For **1**, the two pyrene groups form a partially overlapped excimer despite the existence of the proximal triazacrown ring, which is probably due to hydrogen bondings between the amide groups linked to pyrenes and the amide groups of the triazacrown ring. The intensity ratio of the excimers to the monomers scarcely changed in function of $[I]$ ranged 10^{-7} – 10^{-4} M indicating that the excimer emission at 448 nm results from an intramolecular excimer but not from an intermolecular excimer.

We first of all investigated binding properties of **1** and **2** toward metal ions with respect to fluorescence changes. The results are listed in Table 1. Among metal ions tested, Pb^{2+} and Co^{2+} , known as a quenching metal ion, caused the fluorescence of **1** to be quenched both in the

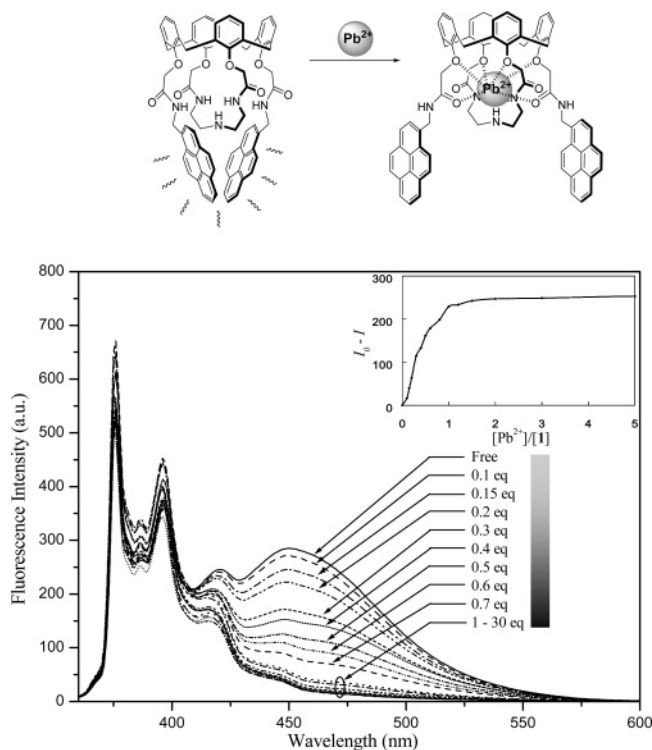


FIGURE 2. Fluorescence changes of **1** ($6.0 \mu\text{M}$) with $\text{Pb}(\text{ClO}_4)_2$ in CH_3CN . The excitation wavelength was 343 nm .

monomer and particularly in the excimer. This is because there are two reasons controlling the fluorescence changes in this system: a heavy metal ion effect^{10b,17} and a reverse PET (photoinduced electron transfer)^{10b,18} from pyrene units to carbonyl groups, of which electron density is decreased by metal ion complexation. This behavior is different from that found by Shinkai et al.¹⁹ and Jin et al.^{7b} They investigated a cone calix[4]arene tetraester with two pyrene pendants in solution and found a remarkable increase of the monomer emission but an excimer extinction upon the metal ion complexation.

Regarding the extinction of the excimer emission of **1**, one can deduce that a conformational change of **1** happens by the metal ion complexation in a way that two outward-facing amide carbonyl groups turns inward to bind to Pb^{2+} . Figures 2 and S1 (Supporting Information) show the fluorescence changes of **1** with various Pb^{2+} and Co^{2+} ion concentrations in acetonitrile, respectively. The fluorescence intensity of the excimer was gradually declined and minimized with 30 equiv of Pb^{2+} and with 20 equiv of Co^{2+} . From these titration experiments, the association constants (K_a) of **1** for Pb^{2+} and Co^{2+} are calculated to be 4.65×10^7 and $4.95 \times 10^6 \text{ M}^{-1}$ in acetonitrile, respectively.²⁰ Pb^{2+} ion complexation not only

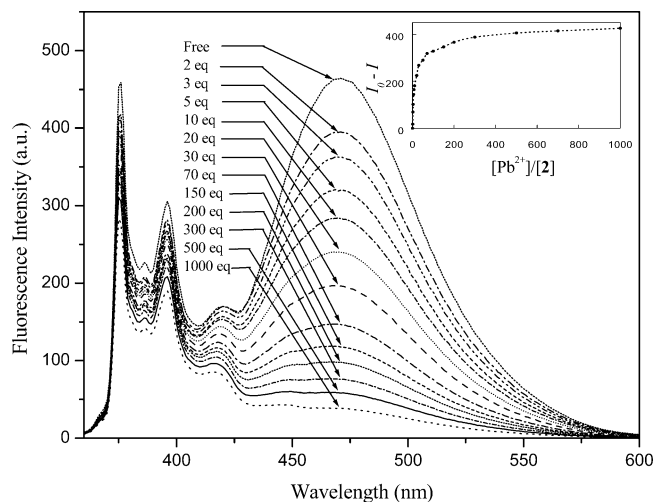


FIGURE 3. Fluorescence spectra of **2** ($6.0 \mu\text{M}$) upon addition of various concentrations of $\text{Pb}(\text{ClO}_4)_2$ in CH_3CN . The excitation wavelength is 343 nm .

TABLE 2. Fluorescence Changes ($I - I_0$) of **1** and **2** upon Addition of Various Tetrabutylammonium anions^a

| ligand | λ_{em} (nm) | fluorescence changes ($I - I_0$) | | | | | | |
|----------|-------------------------------|------------------------------------|-----------------|-----------------|----------------|-------------------------------|----------------------------------|---|
| | | F ⁻ | Cl ⁻ | Br ⁻ | I ⁻ | HSO ₄ ⁻ | CH ₃ COO ⁻ | H ₂ PO ₄ ⁻ |
| 1 | 396 | -308 | -13 | -11 | -96 | -19 | -69 | -35 |
| | 448 | -75 | -38 | -28 | -54 | -35 | -64 | -47 |
| 2 | 396 | -8.0 | 1.0 | -1.0 | -122 | 1.0 | -3.0 | -3.0 |
| | 472 | -25 | -50 | -52 | -61 | 8.0 | -44 | -24 |

^a Conditions: **1** and **2**, $6.0 \mu\text{M}$ in CH_3CN , excitation at 343 nm ; anions, 500 equiv in CH_3CN . I_0 : fluorescence emission intensity of free **1** and **2**. I : fluorescence emission intensity of anion-complexed **1** and **2**.

with pyreneamide but also with triazaamide system was evidenced by ¹H NMR as shown in Figure S3 (Supporting Information). For **2**, we also observed a quenched excimer upon Pb^{2+} ion complexation, which can support the concept that conformational change of the two amide group takes place upon the Pb^{2+} ion binding as mentioned above (Figure 3). Subsequently, the K_a value of **2** is estimated to be $1.2 \times 10^4 \text{ M}^{-1}$.²⁰ Approximately 3800 times higher K_a value of **1** for Pb^{2+} than that of **2** strongly suggests that the triazaacrown ring play an important role in the Pb^{2+} complexation.

In addition to the cation binding properties, we have investigated the sensing properties of **1** and **2** for anions (F^- , Cl^- , Br^- , I^- , HSO_4^- , CH_3COO^- , and H_2PO_4^-) using tetrabutylammonium as a counteranion. The fluorescence intensity changes ($I - I_0$) of **1** and **2** upon addition of anions are listed in Table 2. The results indicate that **1** has a remarkably high selectivity for F^- ion. When F^- ion is added to **1**, the monomer emission was markedly quenched, which is ascribable to the PET effect from the F^- to pyrene units. The excimer emission is also decreased with little change compared to the monomer band. It is attributable to the hydrogen bonding between F^- and the amide groups linked to the fluorophores, keeping the two pyrene units overlapped (see Figure 4). As a result, one can ensure that the F^- ion should efficiently bind to amide hydrogen atoms linked pyrene units with aid of triazaacrown ring. For I^- ion well-known as a quenching heavy anion, both monomer and excimer emission of **1** and **2** were observed to decline.

(17) (a) Chae, M.-Y.; Cherian, X. M.; Czarnik, A. W. *J. Org. Chem.* **1993**, *58*, 5797. (b) Bergonzi, R.; Fabbri, L.; Licchelli, M.; Mangano, C. *Coord. Chem. Rev.* **2000**, *205*, 31.

(18) (a) Ojida, A.; Mito-oka, Y.; Inoue, M.-A.; Hamachi, I. *J. Am. Chem. Soc.* **2002**, *124*, 6256. (b) de Silva, A. P.; Gunarante, H. Q. N.; Lynch, P. M. L. *J. Chem. Soc., Perkins Trans. 2* **1995**, 685.

(19) Aoki, I.; Kawabata, H.; Nakashima, K.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1991**, 1771.

(20) (a) Association constants were obtained using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA, U.K. (b) Connors, K. A. *Binding Constants*; Wiley: New York, 1987.

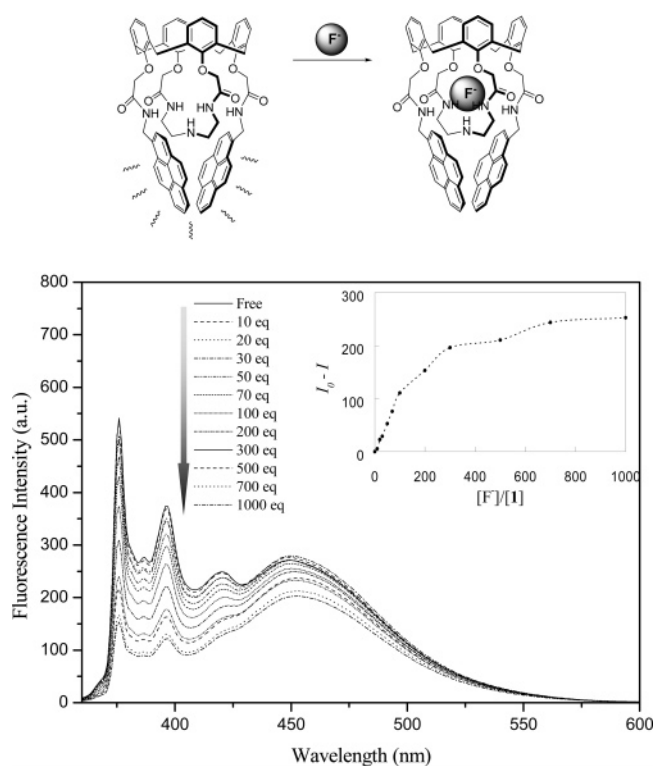


FIGURE 4. Fluorescence emission spectra of **1** ($6.0 \mu M$) upon addition of various amounts of TBA^+F^- in CH_3CN . The excitation wavelength was 343 nm.

Figure 4 shows fluorescence changes with a function of $[F^-]$. From the titration, the association constant (K_a) of **1** is also calculated to be $2.04 \times 10^4 M^{-1}$.²⁰ For **2**, however, the fluorescence intensities are little changed upon addition of the tested anions implying that **2** does not interact with any anions. These results also strongly

indicate that the amide groups of triazacrown ring of **1** play a crucial role in selective binding of F^- ion. The fact is evidenced by 1H NMR peak changes upon the addition of tetrabutylammonium anion salts in $CDCl_3$ that the amide hydrogen atoms of the triazacrown ring participate in F^- ion complexation by H-bonding (Figure S4, Supporting Information). When F^- ion was added to the solution of **1**, the peak of the amide NH was significantly shifted downfield with peak broadening. On the contrary, with other anions, no chemical shift changes for the NH peaks were observed even when more than 10 equiv of the anions were added.

In conclusion, a new fluorogenic calix[4]triazacrown-5 (**1**) bearing two pyrene amide groups was prepared. When Pb^{2+} or Co^{2+} is bound to **1**, the fluorescence intensities are quenched because of a combination of heavy metal effect, reverse-PET, and conformational changes. With the aid of an azacrown unit the two pyrenyl amide groups play an important role in the selective Pb^{2+} ion complexation. Addition of F^- to **1** formed a selective complex through the H-bonding and gave decreasing fluorescence intensity due to the PET effect. So, since compound **1** can function as both cation and anion selective chemo-sensing tools, we believe that this compound can be utilized in many intriguing systems related to the detection of toxic Pb^{2+} or Co^{2+} ion as well as F^- , which are of general interest in the treatment of industrial waste streams.

Acknowledgment. This present research was conducted by the research fund of Dankook University in 2004.

Supporting Information Available: Preparative procedures and analytical data for compounds **1** and **2** and additional fluorescence spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO048228I